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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/757,077	01/14/2004	Lance E. Steward	17355CIP3(BOT)	5352

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EXAMINER	
HAYES, ROBERT CLINTON	
ART UNIT	PAPER NUMBER
1649	
MAIL DATE	DELIVERY MODE
04/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/757,077	STEWARD ET AL.	
	Examiner	Art Unit	
	Robert C. Hayes, Ph.D.	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *09 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,45-51 and 53-60* is/are pending in the application.

4a) Of the above claim(s) *45,46,49-51 and 53-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,47 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,45-51 and 53-60* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/9/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. The amendment filed 11/09/07 has been entered.

2. To clarify the requirement for compliance with the Sequence Rules, no SEQ ID NO is associated with the recitation "MYKD" on pg. 13 (i.e., the last line of *pp* #0051). This recitation appears to be a typographical error, and alternately appears to represent "**N**YKD" at "*position numbers 9-12 of SEQ ID NO: 14*". Accordingly, no new CRF nor paper copy appears to be required. However, appropriate amendment of the specification is required.

3. Applicant's election of Group I (as it relates to botulinum toxin A) in the reply filed on 11/01/06 was previously acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election had been treated as an election without traverse (MPEP § 818.03(a)).

However, newly submitted/amended claims 45-46, 49-51 & 53-60 are directed to inventions that are independent or distinct from the invention originally claimed for the following reasons:

Originally submitted claims were directed to a modified botulinum neurotoxin type A with a modification related to SEQ ID NO: 27, and therefore, could further comprise modifications to the wildtype C-terminus of the light chain of botulinum toxin type A (i.e., SEQ ID NO: 40 (Table 2); as illustrated on pages 65 & 69-73 of the specification). Thus, the elected

invention now only encompasses claims 1 & 47-48, because SEQ ID NO: 40 only contains the generic leucine-based motif of SEQ ID NO: 18 (and specific motif of SEQ ID NO: 1), and does not contain any different generic sequence claimed, etc.

In other words, claims 45-46, 49-51, 53-60 are directed to modifications related to different types of mutations (i.e., SEQ ID NOs: 17, 22, 24, 19, 20, 21, 23 & 5, 7, 10, 12, 2, 3, 8, 9 & 11), which are distinct structural mutations as illustrated by their unique SEQ ID NOs. Therefore, unrelated modifications to that previously claimed are distinct because one is not required for the other to exist.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 45-46, 49-51 & 53-60 are withdrawn from consideration as being directed to a non-elected invention (*which alternatively still constitute new matter*). See 37 CFR 1.142(b) and MPEP § 821.03.

4. The rejection of claims 1-3 & 45-52 under 35 U.S.C. 112, first paragraph for new matter is withdrawn due to either the cancellation or amendment of the claims to now encompass a non-elected invention by original presentation, or due to the amendment of the claims to what is arguably described on pages 65 & 69-73 of the specification, for example.

5. The rejection of claims 1, 3 & 45-52 under 35 U.S.C. 112, second paragraph, as being indefinite and incomplete is withdrawn due to the cancellation or amendment of the claims.

6. Applicant's arguments filed 11/09/07 have been fully considered but they are not deemed to be persuasive.

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 47-48 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4-5 of U.S. Patent No.6,903,187 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because '187 claims a modified BoNT/A *comprising* a leucine-based motif of SEQ ID NO: 2 which increases the half-life of the type A toxin similar to the modified BoTN/A molecules of the instant invention, which also comprise a leucine-based motif of SEQ ID NO: 18. Note that SEQ ID NO:

18 of the instant invention is the same as SEQ ID NO: 2 of '187. SEQ ID NOs: 7, 10 & 12 of '187 are also the same as SEQ ID NOs: 1, 4 & 6 of the instant application.

9. Claims 1 & 47-48 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific modified BoNT/A neurotoxin proteins with a definable sequence change and recited definable and assayable function, does not reasonably provide enablement for any structurally and functionally uncharacterized modified BoNT/A molecules. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for reasons made of record in Paper No: 20070730, and as follows.

Page 71 (*pp* # 287-288) reasonably provides basis for either substituting SEQ ID NO: 39 to the N-terminal end of other botulinum toxins, or that "[o]ne or multiple domains at the N- or C-terminus may be modified by addition, deletion, or substitution". *PP* # 00287 shows that SEQ ID NO: 27 is one such domain within the N-terminal (i.e., a.a.1-30) region of the light chain of BoNT/A (see Table 2, pg. 65; SEQ ID NO: 39). Additionally, the generic leucine-based motif of SEQ ID NO: 18 can be found within the C-terminal (i.e., last 50 a.a.) region of BoNT/A (i.e., SEQ ID NO: 40). However, *pp* 00287 also provides proper context for any different leucine-based motif, as described in *pp* # 113 (i.e., pg. 26 of the specification), in which ΔNΔ8C22 is a distinct and separate modification with different properties versus a leucine-based motif modification (i.e., *pp* #00287; rLC/A (LL→ AA)). No other specific examples of increased biological activity using any specific and structurally definable "leucine-based motif" "within the

C-terminal 50 amino acids of the light chain of BoNT/A are disclosed. No other guidance is provided within the instant specification.

The problem remains that the claims are not limited to modifying the C-terminus of "wildtype" BoNT/A (i.e., SEQ ID NO: 40) due to the recitation of "the terminal 30 amino acids of a light chain from ***a*** botulinum toxin type A (i.e., base claim 1), and that the recitation of "[a] *modified* botulinum neurotoxin type A.... wherein the modification *comprises*..." (i.e., claim 1), or the recitation of "*further comprising a* modification of..." (i.e., claims 47 & 48). Thus, the claims still encompasses random additions, deletions and substitutions to wildtype BoNT/A, and therefore provide insufficient structural characteristics to reasonably enable the currently claimed invention without requiring undue experimentation to determine otherwise; consistent with the teachings of Rudinger previously made of record.

10. Claims 47-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and incomplete for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "further comprising a modification of one or more additional leucine-based motifs of SEQ ID NO: 18 within the C-terminal 50 amino acids of the light chain" is confusing because only one motif of SEQ ID NO: 1 is contained within this C-terminal region, and it is unclear if this one motif is suppose to be changed, or whether multiple additional motifs are to be added (e.g., as it relates especially to SEQ ID NOs: 4, 6 & 13). In other words, "a modification" implies multiple modifications, but it is unclear where they are envisioned to

occur, as currently claimed. Thus, the scope of the claims cannot be accurately assessed, as currently claimed; thereby, being indefinite.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (571) 272-0885. The examiner can normally be reached on Monday through Thursday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Stucker, can be reached on (571) 272-0911. The fax phone number for this Group is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Robert C. Hayes, Ph.D./
Primary Examiner, Art Unit 1649
April 8, 2008